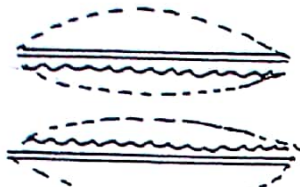


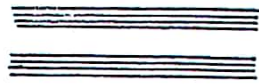
Vascular System

Arteries
Large arteries



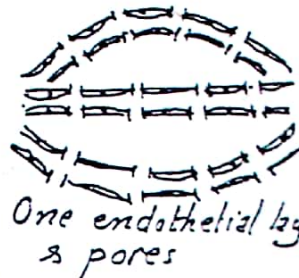
Elastic fibres
Distend & Recoil

Arterioles & Small arteries



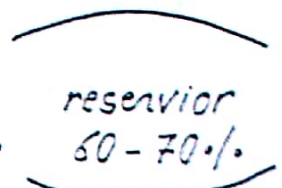
Strong muscular wall

Capillaries



One endothelial layer & pores

Veins



reservoir
60-70%

Thin wall

Forward flow

-- S & D pressure

RESISTANCE

EXCHANGE

CAPACITANCE

V e s s e l s

N.B Lymphatic vs carry plus & large particles from tissues

Vascular endoth. respond to: By secretion of: Which regulate:

- 1 Stretch
 - 2 Blood Flow
 - 3 Circulating substances
- Growth factors Vascular growth
 Vasoactive sub. Vascular tone

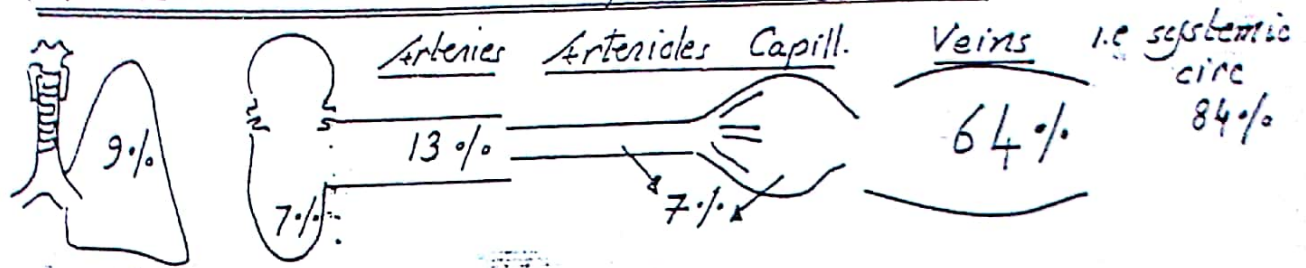
Endothelium is involved in homeostasis & immune reactions

<u>Vasodilators</u> : - Nitric oxide ✓ NO - Prostacyclin ✓ PG₁₂	<u>Vasoconstrictors</u> : - Endothelin-1 ET₁ - Angiotensin II
<u>Anti thrombotic</u> : - TPA ✓ - Prostacyclin ✓ PG₁₂	<u>Pro thrombotic</u> : - Plasminogen activator inhibitor 1 PAI₁ - Thromboxan A₂
<u>Growth inhibitors</u> : - Nitric oxide NO - Transforming growth Factor-β	<u>Growth stimulators</u> : - Vascular endoth. growth factor - Angiotensin II
<u>Anti inflammatory</u> : - Nitric oxide NO	<u>Pro inflammatory</u> : - Tumour necrosis factor-α

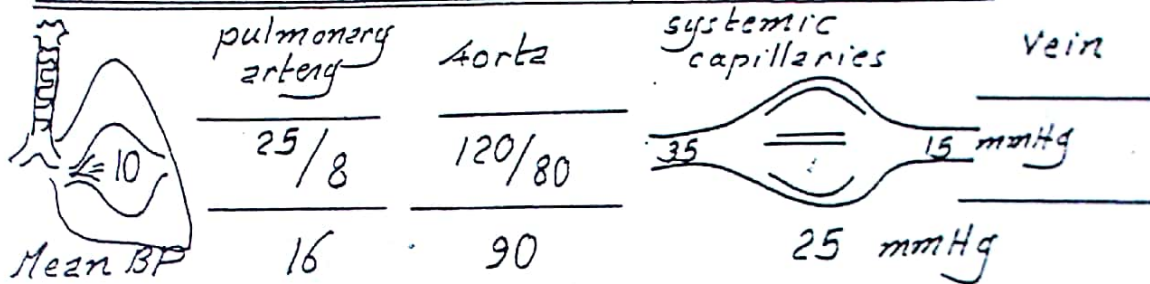
VISIT...

LANZAROTE
Caliente.COM

Volume of blood in different parts of circulation :

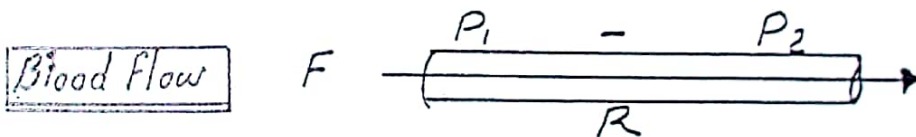


Pressure of blood in different parts of circulation :



Mechanical Forces acting on bl. vs wall

- 1 Pressure perpendicular force compressive stress mmHg
on a surface
- 2 Tension parallel stretching force tensile force Newton
to the surface
- 3 Shear stress tangential drag force shear stress 20-40 dyne/cm



- Definition vol of blood crosses a point per unit time
- Relationship of F (Flow), ΔP (pressure gradient) & R resistance

A) $F = \frac{\Delta P}{R}$

B) $R \propto \frac{L \eta}{r^4}$ r radius of vessel
 L length of "
 η viscosity of blood

• Poiseuille Hagen Formula

From A & B

$$F = \frac{\pi \Delta P r^4}{8 \eta L}$$

π and 8 are constant

r IF r $\uparrow \uparrow 20\%$ $\rightarrow R$ $\downarrow 50\%$ $\rightarrow F$ $\uparrow \uparrow 200\%$

12/08/25

Viscosity depends on

Plasma ptns
RBCs

s ++

e.g ++ immunoglobulins
e.g rigid RBCs as in hereditary spherocytosis

- Measurement of bl. Flow Ultrasonic Doppler Flowmeter.

- Calculation of resistance in: $R = \frac{\Delta P}{F}$
Systemic circulation Pulmonary circulation

$$R (TPR) = \frac{MAP - RAP}{COP}$$

$$= \frac{90 - 0}{5}$$

$$= 18 \text{ mmHg/L/min}$$

$$R (Pul R) = \frac{MPP - LAP}{COP}$$

$$= \frac{15 - 8}{5}$$

$$= 1.4 \text{ mmHg/L/min}$$

- Velocity of bl flow in s cross sectional area (cm²)

Aorta Small arteries Arterioles Capillaries Venules Small veins Vena cava

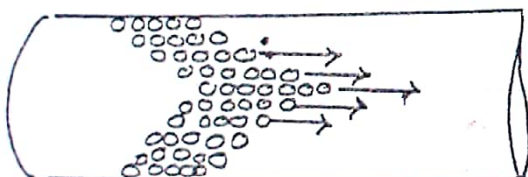
Area 2.5 20 40 2500 250 80 8 cm²

Velocity 0.5 meter/s

0.5 mm/sec.

- Types of Flow

Laminar (streamline)



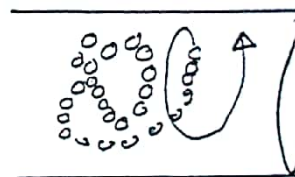
Silent

critical velocity

Turbulent F

is related to

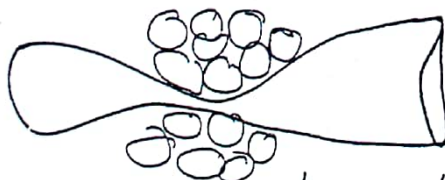
Velocity of bl
Viscosity of bl.
Diameter of vs



Sounds

e.g Korotkoff's
Anaemia

Critical closing pressure



tissue P >> blood P = 15 mmHg

Systemic arterial compliance

$$C = \frac{\Delta V}{\Delta P}$$

Mainly by aorta & large arteries

2 Functions:

- 1 Continuous flow
- 2 -- Cardiac work

2012/08/25

3

Laplace law

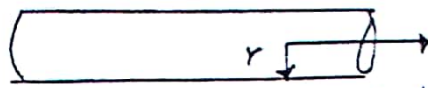
- 1 In a cylinder e.g. bl. vessel



Wall tension (T) = transmural pressure (P) $\times$ radius of vessel (r)

$$T = P \times r$$

$$P = T/r$$



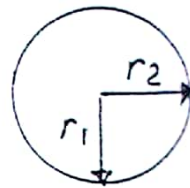
In capillaries, r is small so less T is needed to balance the distending pressure

So capillaries can withstand high P without rupture.

- 2 In a sphere e.g. viscus

$$P = T/r_1 + T/r_2 \quad r_1 = r_2$$

$$P = 2T/r$$



- 3 In a thick walled structure e.g. Lt ventricle

$$S \text{ wall stress} = \frac{T}{w} \quad \begin{matrix} \text{tension} \\ \text{wall thickness} \end{matrix}$$

$$P = 2T/r$$

$$2T = Pr$$

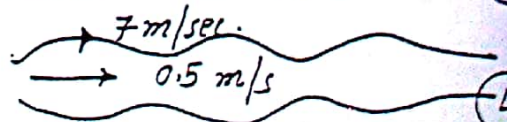
$$T = Pr/2$$

$$S = Pr/2w$$

Arterial blood pressure

• Definitions:

- ABP Pressure of Blood on Arterial wall
- Systolic BP Peak P during Systole 120 (90-140 mmHg)
- Diastolic BP Lowest P " Diastole 80 (60-90 mmHg)
- Mean ABP = Diastolic P + $1/3$ pulse P = 90 mmHg
It is close to " P because Diastole > Systolic time
- Pulse P = Systolic P - Diastolic P = 40 (30-50 mmHg)
It is the cause of arterial pulse



• Factors that determine mean ABP & PP

$$\Delta P = F \times R$$

$$ABP - Rt AP(0) = COF \times TPR$$

$$ABP = COF \times TPR$$

$$ABP = HR \times SV \times TPR$$

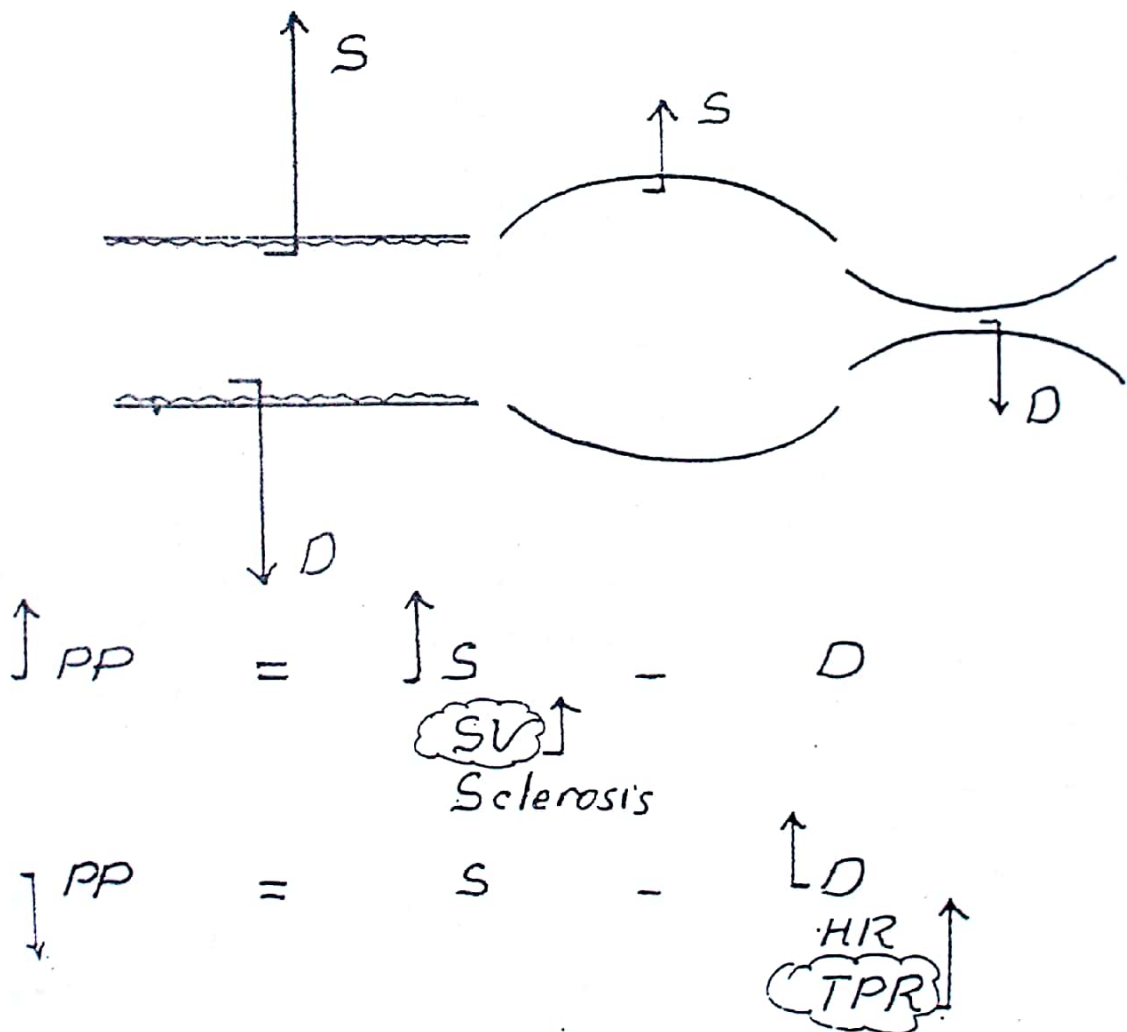
①

②

③

④ Arterial compliance

Atherosclerosis $\longrightarrow$ -- arterial compliance.



⑤

• Physiological variations in ABP

① Age

	S	D
- newly born	80	40
- 4 years	100	65
- adult	120	80
- 60 years	140	90

② Sex

♂ > ♀
Before
menopause

Primary determine of sys. volume $\rightarrow$ SV
dys. P $\rightarrow$ TPR.

③ Race

Americans &
Europeans >
orientals

④ motions
⑤ exercise $\rightarrow$ ABP

Systolic P
isotonic cont ++ (++SV)
isometric cont. ++

⑥ Circadian rhythm

Peak: early morning
Lowest: midnight
Cause: symp activity changes
Variations: 15 - 25 mmHg

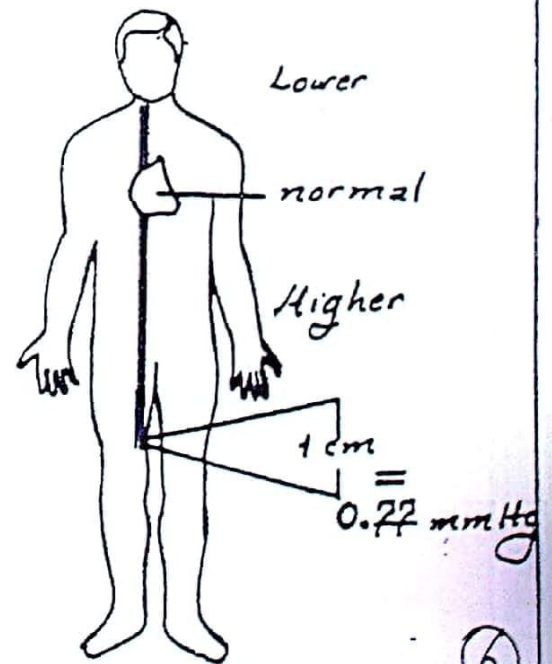
⑦ Respiration

- Traube Hering waves
- At beginning of insp. ABP -
Lung inflation Reflex $\xrightarrow{\text{vagus}}$ VD
 - At end of insp. & start of exp
ABP is maximum

(++ tension $\rightarrow$
VC $\rightarrow$ ++TPR.)
(same P) (same defacto)
or
Diastolic P
-- or $\pm$ (-- TPR)
++ VC $\rightarrow$ (TPR $\uparrow$), DTP $\uparrow$

⑧ Gravity

no effect on lying down



⑥

Capillary circulation

Capillary blood flow

VASOMOTION

• intermittent

Sympathetic

Metarteriole

smaller muscle wall
terminates in true capill

Precapillary sphincter

little smooth ms
surrounds true capill

Thoroughfare vessel
connects metarteriole
directly with venule

Pericyte

long process
endoth. junction
contractile & release
vasoactive subst.

Venule

open by
metabolites

++ CO₂
-- O₂
H⁺
Lactic acid

Metarteriole

Precapill. sphincter

6 - 12 / minute

close by
sympathetic

very slow

5000 cm²
Capillaries
1000

0.5 mm / second

5 cm²
Aorta
1

0.5 meter / second

Cir

12/08/25

- Equilibrium with interstitial fluid (Capill. exchange)
3 mechanisms:
 - 1 Diffusion most important
 - 2 Trans-capill. filtration (Bulk Flow)
 - 3 Vesicular transport (pinocytosis + exocytosis)

Diffusion most important
Factors affecting DR

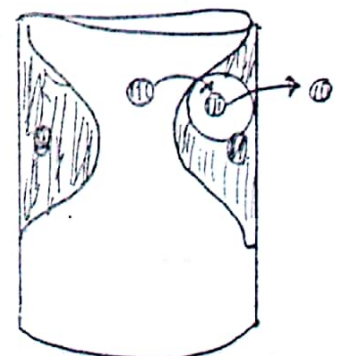
A) Factors related to capillary permeability 3

<u>Permeability</u>	<u>Capill. wall</u>	<u>Endothelial cells</u>	<u>e.g</u>
1 <u>High</u>	Discontinuous	Large gaps	
2 <u>Low</u>	Continuous	Tight junct.	
3 <u>Moderate</u>	Fenestrated	Pores (fenestrae)	

B) Factors related to substances 3

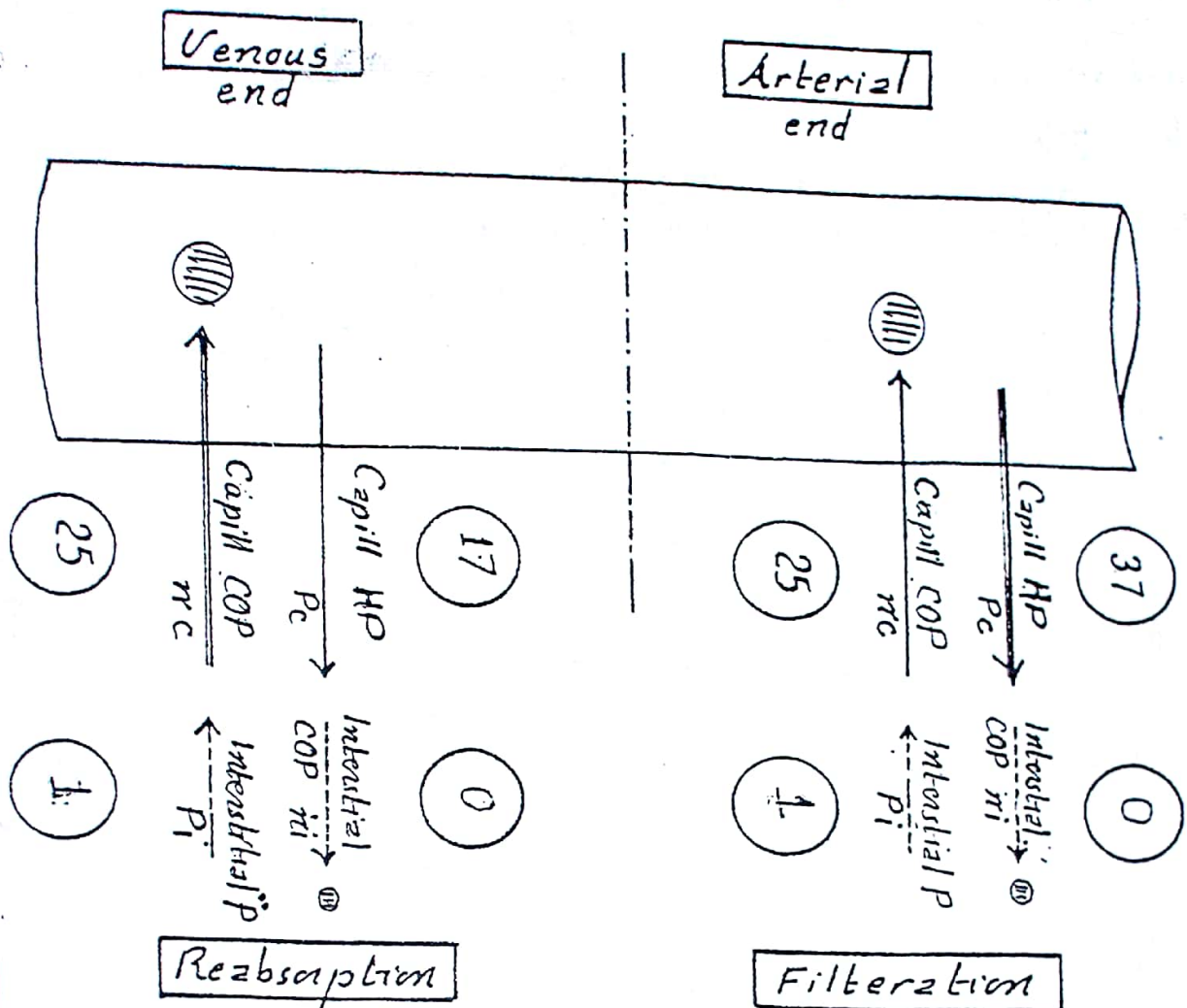
- 1 Concentration gradient $DR \propto C_1 - C_2$
- 2 Lipid solubility $DR \propto \text{solubility}$
 Lipid soluble sub. diffuse via cell membrane & pores
- 3 MW $DR \propto \frac{1}{MW}$
 This is important for H_2O soluble subst

Vesicular transport
 Large Lipid-insoluble molecules
 e.g ptns (antibodies)
 cytokines
 ptn bound hormone



Trans-capillary Filtration (Bulk Flow) Starling forces

Depends on balance of $\begin{cases} \nearrow \text{Hydrostatic } P \text{ gradient} \\ \searrow \text{Osmotic } P \text{ gradient} \end{cases}$



-9 mmHg net Force
 85% of Filtered Fluid vol.
 15% via lymphatics

11 mmHg
 24 L/day
 i.e 0.3% of COP

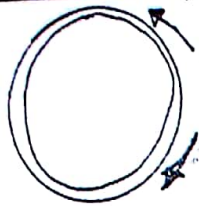
$$\text{Fluid movement} = K [(P_c + \pi_i) - (P_i + \pi_c)]$$

K (Capill filtration coefficient) $\propto$ permeability and area.

N.B Along entire length of capill Fluid moves OUT in kidneys
 " " " " " " IN in intestine & lungs 9

- Capillary pressure & capillary fragility

- Because of Laplace law, capillaries withstand high P



$$T = P \times r$$

very small

- Causes of capillary fragility

Defect in

- | <u>Capillary wall</u> |
|---------------------------------|
| 1 Vitamin C deficiency (scurvy) |
| 2 Old age |
| 3 Some allergic conditions |

<u>Blood</u>
Thrombocytopenic purpura

- Capillary reactions

White reaction (line)

Light stroking

Capill VC

Cause Mech. stimulation of precapill sphincter

Triple response

Firm stroking or insect bite

[1] Red line site Capill VD Direct 10 seconds

[2] Wheal site ↑ Capill Chemical permeab. histamine, bradykinin, substance P

[3] Spreading around Arteriolar Antidromic Plate VD impulses

- Angiogenesis

Developing new vessels by $\left\{ \begin{array}{l} \text{migration} \\ \text{proliferation} \end{array} \right.$ of endothelium

Main mechanism to form new vessels in adult

Mechanism: ischaemia $\xrightarrow{\text{stim}}$ endothelium $\rightarrow$ VEGF
vascular endothelial growth factor

(10)

21/08/25

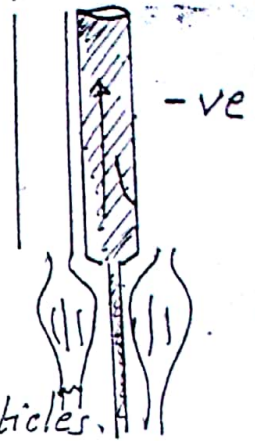
Lymphatic circulation

Normal lymph flow is 2-4 L / day
Loose junction between endoth. cells

Lymph drainage is helped by :

- 1 contraction of
- 2 skeletal ms
- 3 Valves allow only one direction.
- 4 -ve intrathoracic p
- Arterial pulsation

smooth ms of lymphatics



Functions of lymphatics

- 1 Return of
- 2 Ptns and large particles, 25%.
- 3 Excess filtered fluid.
- 4 Absorption of fat 80% Long chain f.a & cholesterol.
- 5 Removal of bacteria

Factors that determine vol. of interstitial fluid (ISF)

A) Capillary factors

- 1 Hydrostatic P
- 2 Capillary Osmotic P
- 3 Filt. coefficient
- 4 Number of active capill.
- 5 Ratio of pre to post capill. resistance

B) Other factors

- 1 ISF pressure
- 2 Lymph flow
- 3 Total ECF volume.

Edema

Defin. Abnormal large ISF volume.

Gravity * Lower limbs in standing position
Back in recumbent position.

Causes

1 ++ Filtration P 2 -- osmotic P 3 ++ Capill permeab 4 lymph. obstruct.

a Arteriolar dilat.

a Nutritional

a substance P

a Elephantiasis

b Venular constrict.

b Liver cirrhosis

b Histamine

b Cancer cells

c Venous P

c neptrosis

c Kinins

c Removal

- Heart Failure (RT)

- Venous obstruct.

- Incompetent valve

- inflam.

- allergy

- burns

Venous circulation

Functions: 1 Transport vessels 2 Capacitance vessels

Central venous pressure CVP

- Definition Rt atrial pressure

- Normal 0 - 2 mmHg

- Significance

1 Ventricular filling (main force)

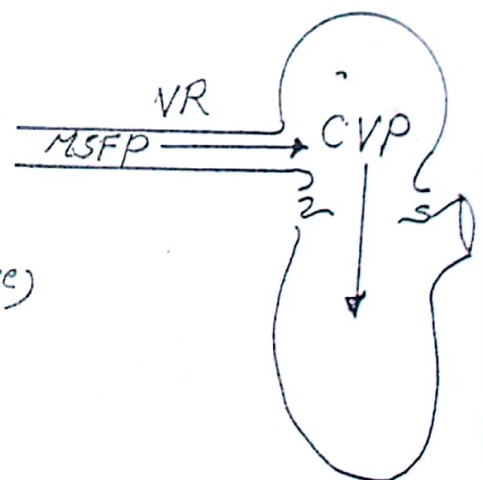
2 VR $\propto$ MSFP - CVP

3 Index of blood volume

- Changes

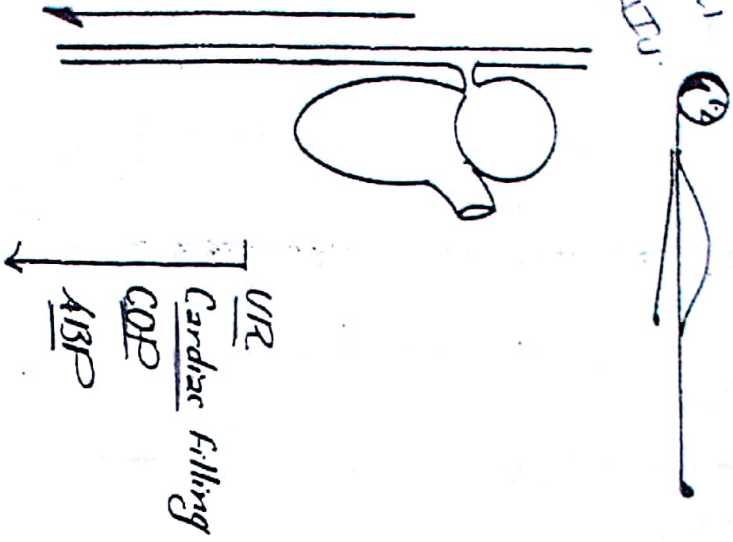
4 -- Age

5 ++ Rt sided H. failure.

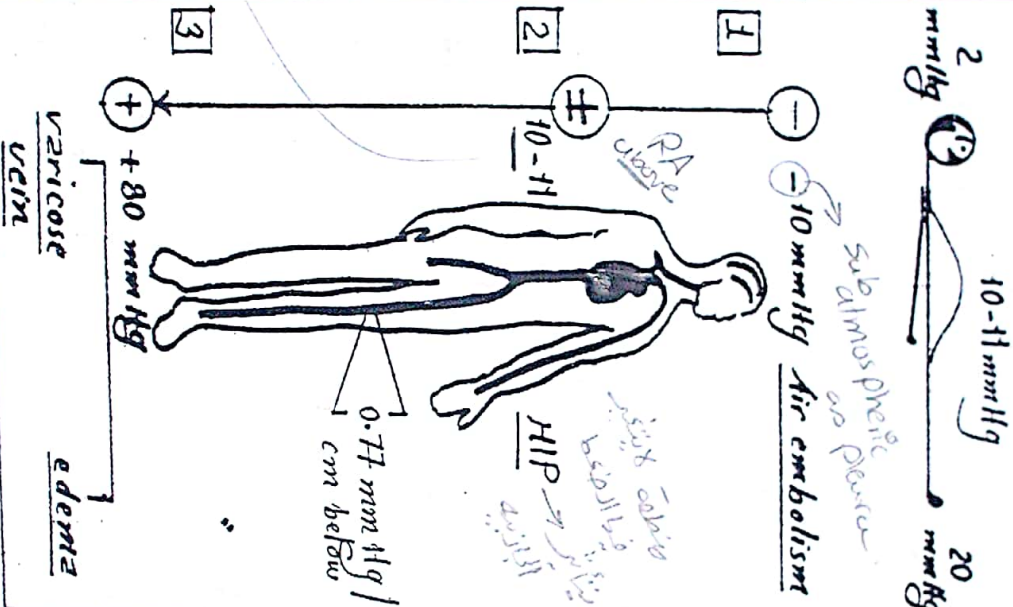


Effects of gravity on venous circulation

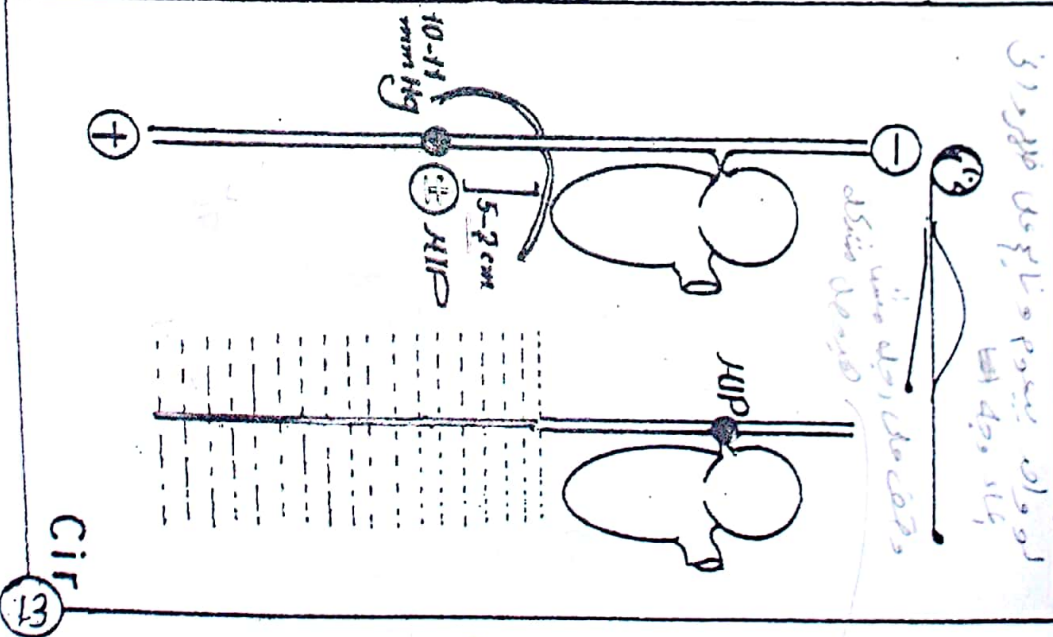
Orthostatic hypotension



P in different veins



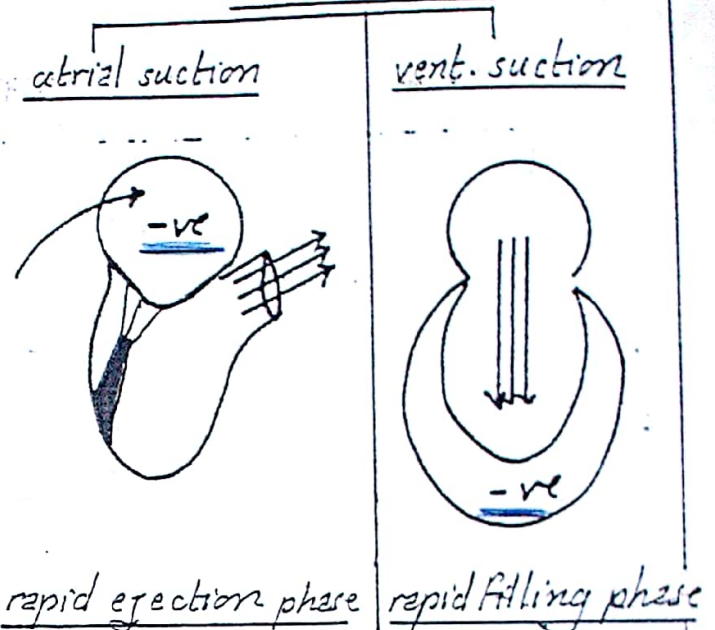
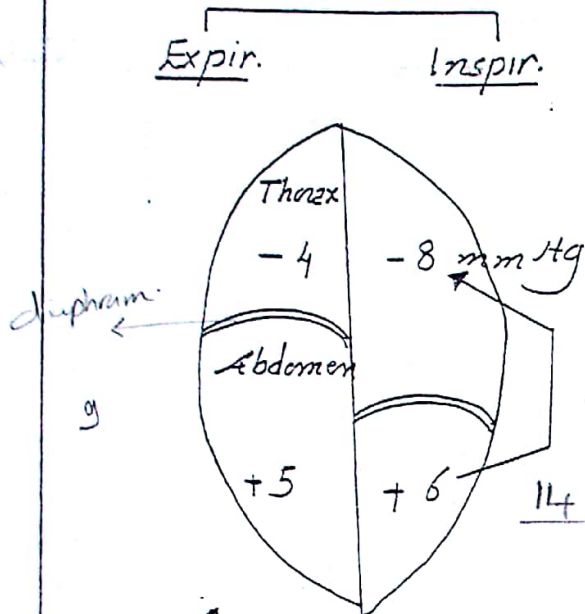
Hydrostatic indifferent point



Mechanisms help venous return upwards towards the heart

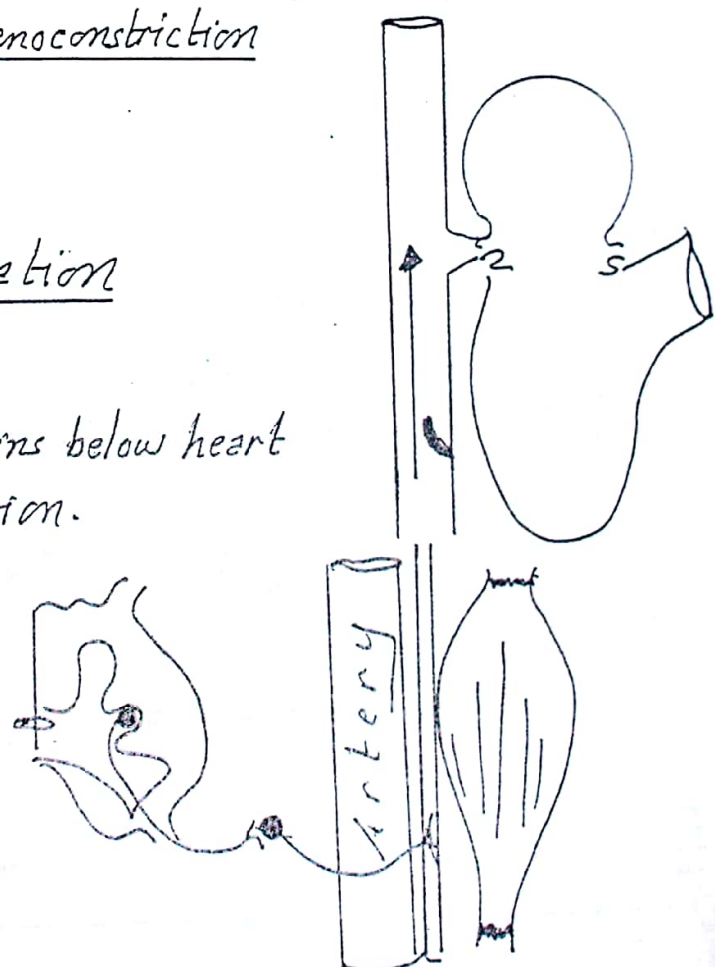
i.e. help VR against gravity

- ① Thoracic pump (suction)
- ② Heart beat effects
Cardiac suction



- 3 Sympathetic venoconstriction
- 4 Muscle pump
- 5 Arterial pulsation

⑥ Valves
Only in veins below heart
One direction.



Basic mechanisms of circulatory control

Aim of circulatory control

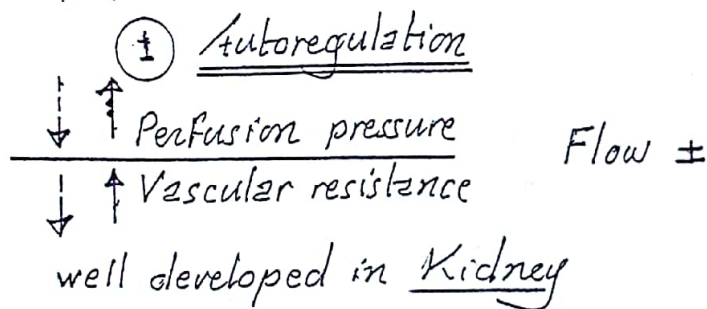
- 1 ++ bl. flow to active tissues.
- 2 maintain bl. flow to heart and brain in hge.
- 3 ++ or -- heat loss by redistribution of blood.

Circulatory adjustments occur by change in

- 1 COP
- 2 Vol of blood in capacitance vessels (veins)
- 3 Diameter of resistance " (arterioles)

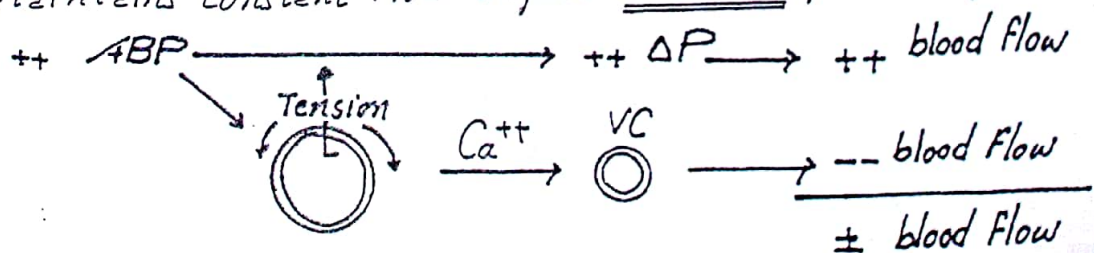
Regulation of diameter of arterioles

- Local [1 Local regulatory mechanisms (autoregulation)
2 substance secreted by endothelium.
- Systemic [3 Circulating vasoactive substances
4 Nerves



A) Myogenic autoregulation

Maintains constant flow despite INCREASE perfusion pressure



B) Metabolic autoregulation

Maintains constant flow despite DECREASED perfusion pressure

-- Perfusion $\longrightarrow$ ++ vasodilator metabolites
 $\longrightarrow$ relaxation of arterioles & precapill. sphincters $\longrightarrow$ ++ Flow

Vasodilator metabolites

- 1 -- O_2 tension (Hypoxia)
- 2 ++ [H] by acidic metabolites e.g. lactic acid.
- 3 ++ PCO_2 (Hypercapnia)
- 4 ++ osmolality (Hypertonicity)
- 5 ++ body temp.
- 6 ++ K^+ especially in skeletal ms
- 7 ++ Adenosine " in cardiac muscle.
- 8 Histamine in injured & inflamed tissues.

VB Active hyperaemia

++ Tissue activity

VD occurs during

Reactive hyperaemia

++ Tissue activity
and obstruction of bl. vessel

VD occurs after

② Substances secreted by endothelium

A) Nitric oxide (NO)

- Formation: L-arginine $\xrightarrow[\text{(eNOS)}]{\text{NO synthetase}}$ NO

- Stimuli: Acetylcholine
Bradykinin
Shear stress
ABS

- Mechanism: paracrine action cGMP via guanylate cyclase.

- Importance:

- 1 Regulation of coronary, cerebral & pulm. circulations
- 2 VD of penile arterioles $\longrightarrow$ erection
- 3 Continuous release maintains normal ABP

NO is reduced in hypertension

B) Endothelins ET 3 types most potent ①

- 1 Endothelin 1 primary type most potent VC
- 2 " 2 in kidney & intestine
- 3 " 3 in brain

⑩

012/08/25

- Endothelin receptors Serpentine receptors.

1 ETA for ET₁ 2 ETB for ET₁, 2 & 3.

- Cardiovascular action of ET₁

1 VC : ET₁ via ETA → Ca influx → VC

2 veins > arterioles

3 Coronary VC

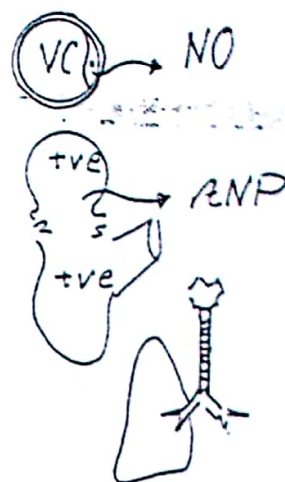
4 Renal VC → -- GFR

5 Heart +ve inotropic & +ve chronotropic

6 Release of NO via ETB (G₁₂, & G₁₃)

7 Release of ANP, renin, aldosterone & catecholamine

8 Pulm. bronchoconstriction



- ++ By ET₁ secretion -- By

1 Angiotensin II

2 Catecholamines

3 Vasopressin

4 Hypoxia

5 Thrombin

6 Shear stress

↑↑↑
Vasoconstrictor
Hormone

↓↓↓
Dilators

1 NO

2 ANP

3 Prostacyclin

Prostacyclin

- Formation by endothelial cells from arachidonic acid.

- Functions
 - 1 VD
 - 2 -- platelet aggregation.

- Relation ++ NO release → potentiates prostacyclin

③ Systemic Regulation by hormones

Vasoconstrictor hormones

1 Vasopressin

2 Angiotensin II

3 Epinephrine

4 Norepinephrine

Vasodilator hormones

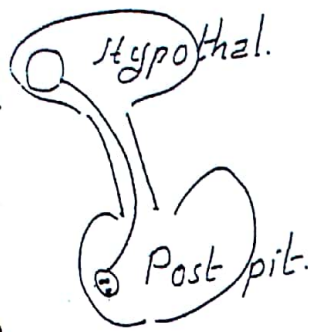
1 Kinin

2 Natriuretic peptide

2012/08/25
17

Vasopressin (Antidiuretic hormone ADH)

• Formed:



• Stored:

• Stimuli:

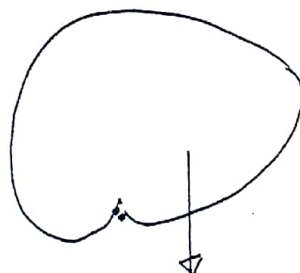
- 1 ++ osmolarity of ECF by 1%
- 2 -- BI volume by 10%
- 3 Angiotensin II

• Actions:

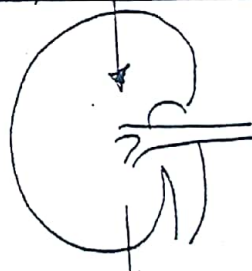
- * VC → V₁ R
- * ↓ excretion of water → V₂ R

Renin - Angiotensin System RAS

Renal ischaemia
Hypovolaemia -- ABP
-- Na⁺ in DCT
Symp. stim. (B₁)



Angiotensinogen
(Alpha globulin)



RENIN
proteolytic enzy

Angiotensin I
(Decapeptide)

Angiotensin I

ACE
> 40% in blood

Angiotensin II

via AT₁

via AT₂



Salt & H₂O reabsor.

Arterioles

Veins

Direct

Adosterone

Others

1- ++

ADH

3 ++

catecholam.

2 ++

Thirst

4 --

Renin

1 V₁ D

2 Diuresis

3 Natriuresis

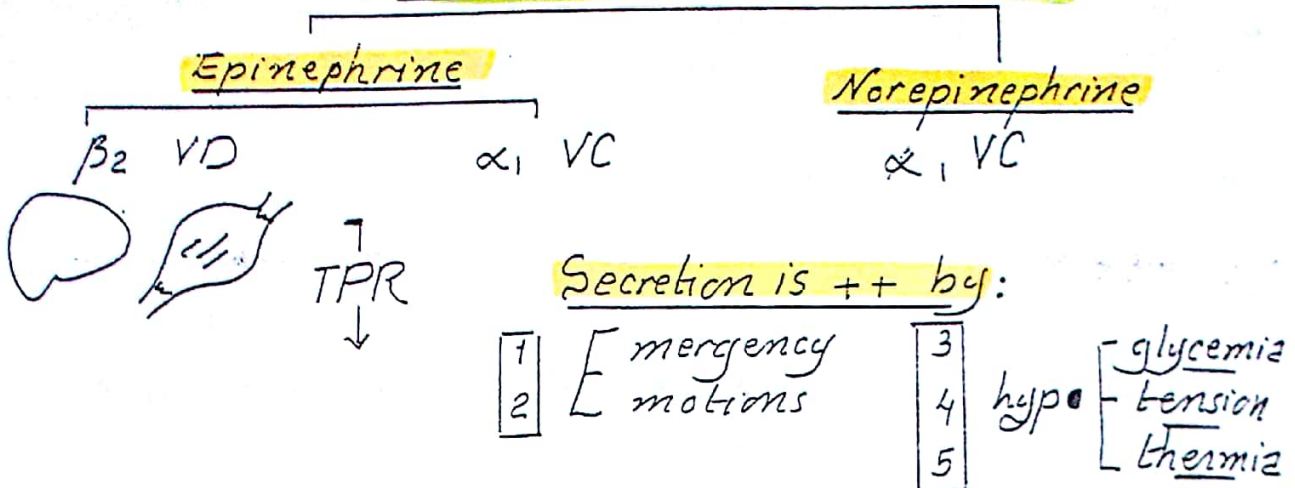
4 Apoptosis

Note Angiotensin III

100% Aldosterone

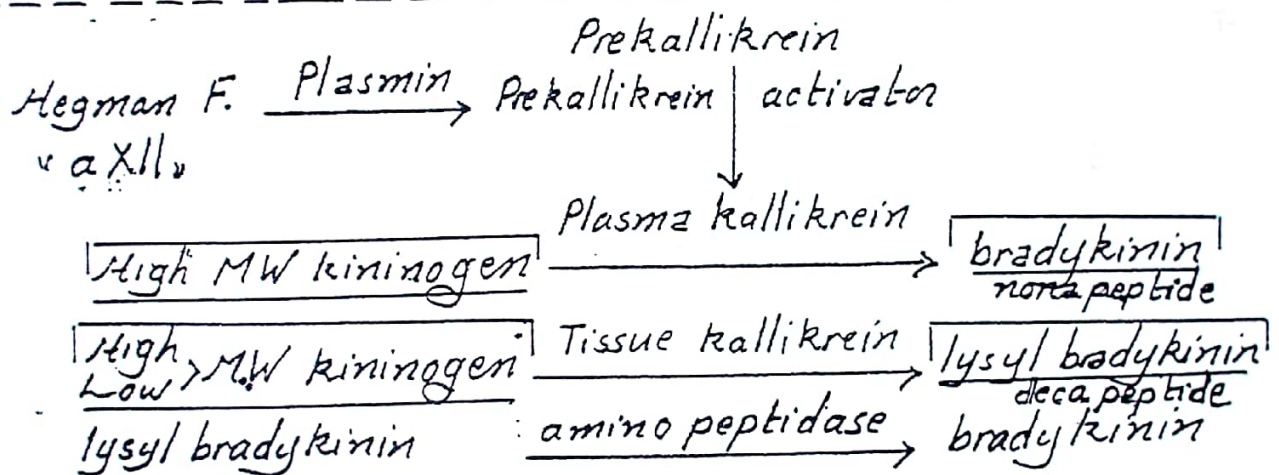
40% VC of II

Catecholamines (Adrenal medulla)



Kinins

2 Kininogens $\xrightarrow{2 \text{ kallikreins}}$ 2 Kinins 2 receptors 2 Kinases



Destruction: Kinase I & Kinase II (ACE)

Receptors: β_1 & β_2

- Functions Mostly β_2
- 1 Relaxation of plain muscles of blood vessels
 - 2 Contraction of plain muscles of viscera
 - 3 ++ Capillary permeability
 - 4 +ve Chemotaxic effect
 - 5 Stimulation of pain receptors via β_1

Natriuretic hormones

- 3 A, B & CNP
- Types 1 Atrial natriuretic peptide ANP From atrial m.ocytes
 - 2 Brain " " BNP " vent. " & brain (B)
 - 3 C type " " CNP " endoth. cells of " & kid.

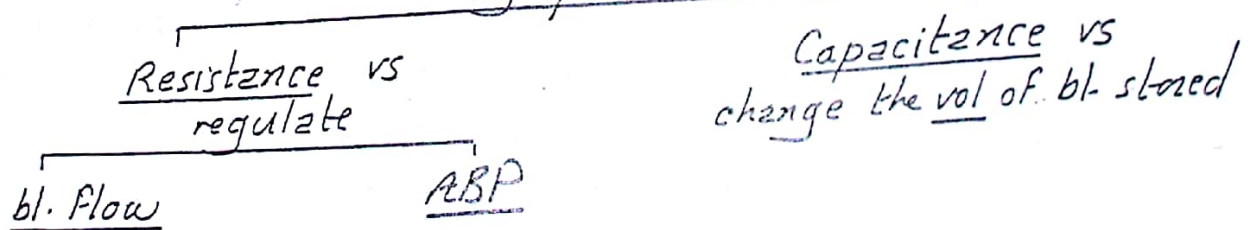
- Three types of receptors:
 NPR A
 B
 C

Has greatest affinity for
 A NP
 B NP
 A, B, C NP

- Three main actions:
 -- bl vol $\rightarrow$ -- CVP, -- COP & -- ABP.
 Antagonises the effect of RAS on ABP. viz
- ④ VASCULAR action ③ RENAL action ⑤ ADRENAL action
 1 VD via cGMP 1 ++ Na⁺ excretion -- aldosterone secretion
 2 VC of catechol. 2 Prorenin $\rightarrow$ renin
 3 VC of angiot. II 3 -- aldosterone action
- Natriuretic secretion is increased by:
 1 Stretch of atrial muscle fibres e.g ++ ECF
 2 Symp. stimulation
 3 Sodium conc. in ECF ++
 4 Angiotensin II
 5 Endothelin

④ Systemic regulation by the nervous system.

All vessels (except capill. & venules) receive sympathetic nerves
 Sympathetic fibres



A) Vasoconstrictor Fibres

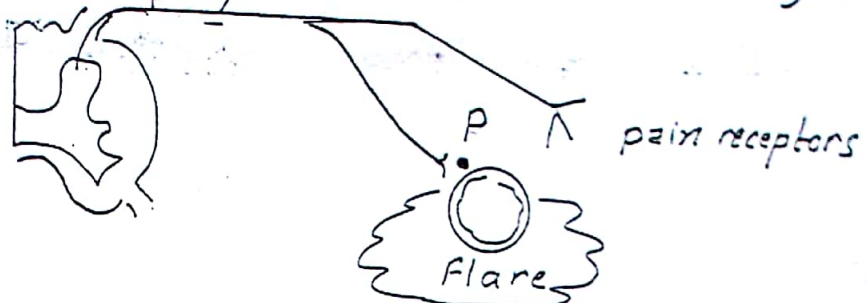
Sympathetic noradrenergic α receptors

Most bl. vessels

Tonic activity (vasomotor tone) maintains <

B) Vasodilator Fibres

- Sympathetic cholinergic to sk ms
- Parasympathetic erectile tissue
- Antidromic impulses (Local axon reflex)



Regulation of ABP

skin
limbs
abdominal

Ventricle
spleen
adrenal medulla

Rapid

Seconds to minutes

Nervous reflexes

Intermediate

Minutes to hours

- 1 Capill. fluid shift
- 2 Stress relaxation
- 3 RAS

Long term mechanisms

Days

- 1 Renal P natriuresis
- 2 Aldosterone

Nervous (rapid) regulation

Medullary centres:

Cardiac inhibitory area

Dorsal motor nucleus of vagus
in nucleus ambiguus

Vaso motor area

rostral ventrolateral medulla (RVLM)

++ symp tone

VC

Heart

RA, BP

Arterioles

Veins

++ TPR

++ VR, COP

++ COP

$$ABP = TPR \times COP$$

-- vagal tone

(21)

Afferent to medullary cardiovascular areas

① Arterial baroreceptors

High P baroreceptors

Site carotid sinus
aortic arch

Innervation - Buffer nerves
carotid sinus n. (IX)
aortic n. (X)

Stimulus
ABP 50 - 160 mmHg

Functions

Baroreceptor reflex
maintains ABP

Note

Carotid sinus syndrome



Major cause - when ABP ↑, peripheral chemoreceptors & 50% ABP cut-off, 50% peripheral work again

② Peripheral chemoreceptors

Site carotid bodies
aortic bodies

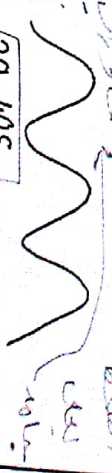
Innervation Buffer nerves

Stimulus ↓ PO₂ ↑ PCO₂ ↑
i.e. ABP below 50 mmHg
PO₂ = 100 mmHg

Response - HR

Overall effect ↑ ABP
HR

Major waves



Direct effect of ↓ PO₂ ↑ PCO₂

Cushing reflex

↑↑ intracranial P = ↑↑ ABP
- - - - - HR

↑ HR 20-30 times

$$ABP = (PPR) \times Flow$$

(سوال 3)
 ③ Atrial (volume) receptors = Cardio-pulm. stretch receptors
Low pressure receptors

Site Atria at vein entrances

Innervation Vagus

Stimulus Distension

e.g. ++ CVP due to $\left\{ \begin{array}{l} ++ VR \\ ++ bl vol. \end{array} \right.$

Functions

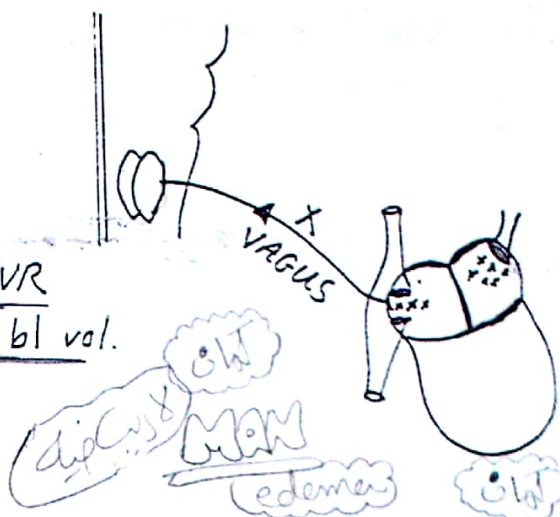
Atrial volume reflex

a Systemic VD

b ++ HR Bainbridge reflex if initial HR is slow

c -- Vasopressin → slow & gl. con.

d ++ ANP → slow & gl. con.



④ Lt ventricles
Coronary Chemo reflex

Site wall of Lt ventricle

Innervation V A G U S

Stimulus 1 - Marked stretch

2 - Injection of some drugs (e.g. serotonin, veratridine) in Lt coronary artery

Response Transient apnea followed by rapid breathing

N.B

Both are mechano & chemoreceptors
 Bezold Jarish reflex

⑤ Lung J receptors
Pulmonary Chemoreflex

C fibre endings close to pulm. vs.

Hyperventilation (+VR)

Pulm edema, embolism or congest.

⑥ Higher brain centres

CC (limbic lobe & prefrontal area) → Hypothalamus

At beginning of exercise: 1 ++ HR & ++ ABP

2 VD of sk ms arterioles

⑦ Somatic afferents

a Pain receptors

① Cutaneous

++ HR ++ ABP & Adrenaline release

② Visceral

-- HR -- ABP

b Thermal receptors

① Cold

afterload ++ ABP

② Hot

-- ABPVD

c Proprioceptors

m. exercise

++ HR ++ ABP

Intermediate mechanisms

① Stress relaxation

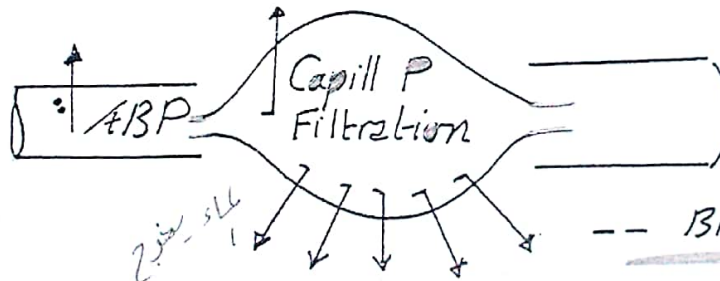
related to viscoelastic (not contractile) properties.

Minimised P changes with bl. volume changes

Mechanism: Law of Laplace

Importance: wall tension not -- radius. Defense against sudden change in bl. volume.

② Capillary Fluid shift mechanism



③ RAS

Angiotensin II is formed in 20-30 min

Discuss

Long term mechanisms

Renal body fluid mechanism:

It controls ABP by adjusting vol. of ECF & in turn VR, COP & ABP. ECF volume is maintained by regulation of renal Na^+ & H_2O excretion.

① Renal p natriuresis

basic & most powerful of long term mech.

++ ABP → ++ Na^+ & H_2O excretion → -- ECF vol. → -- ABP

b) Renin - angiotensin aldosterone system

-- ABP $\rightarrow$ ++ Angiotensin II $\rightarrow$ ++ Na & H₂O reab. via
 a Direct action
 b Aldosterone secretion] $\rightarrow$ ++ ECF vol. $\rightarrow$ ++ ABP

c) ANP

++ ECF vol $\rightarrow$ ++ ANP secretion $\rightarrow$ -- Na & H₂O reab.
 $\rightarrow$ ++ P natriuresis

d) Vasopressin

-- ECF vol $\rightarrow$ -- discharge of atrial (low pressure) receptors
 $\rightarrow$ ++ vasopressin secretion $\rightarrow$ ++ H₂O reab $\rightarrow$ ++ ECF vol.

vascular
hr 50:00

Hypertension HTN

● Definition: sustained ++ of systemic ABP < Systolic > 140 mmHg
Diastolic > 90 "

● Types & causes: 2 types

1 Essential (primary) HTN 93-95%.

Unknown cause

2 Secondary

HTN 5-7%.

Known causes

<u>Renal causes</u> ^{salt + water}	<u>Suprarenal (endocrinal)</u> ^{هرمون}	<u>Drug induced</u>	<u>Coarctation</u>
1 <u>Chronic renal failure</u>	1 <u>1ry hyperaldosteronism</u>	1 <u>Nonsteroidal antiinf of aorta</u>	
2 <u>Renal artery stenosis</u> ^{Renal ischaemia}	2 <u>Cushing</u> (++) <u>cortisol</u>	2 <u>Glucocorticoids</u>	
	3 <u>Pheochromocytoma</u>	3 <u>Contraceptive pills</u>	

● Prevalence rate in Egypt $\rightarrow$ above 25 y 26.3% above 60 y 50%

● Classification of HTN

				<u>Mild</u>	<u>Moderate</u>	<u>Severe</u>
<u>Category</u>	<u>Optimal</u>	<u>Normal</u>	<u>High normal</u>	<u>Grade 1</u>	<u>Grade 2</u>	<u>Grade 3</u>
<u>Systolic</u>	<120	<130	<139	<159	<179	>180
<u>Diastolic</u>	<80	<85	<89	<99	<109	>110

● Diagnosis of HTN:

at least 5 office visits over days to months

accurate measure of ABP under standardized conditions

(25)

2012/08/25

also called as cushing reflex $\leftarrow$ 2 things $\leftarrow$ Bainbridge reflex

Control of HR

Stimuli $\Rightarrow$ ++ HR, ++ ABP

Stimuli $\Rightarrow$ -- HR, -- ABP

Exceptions 1 Atrial stretch R $\rightarrow$ -- ABP & ++ HR
2 ++ intracranial P $\rightarrow$ ++ ABP & -- HR

- HR is increased by
 - activity of arterial barorec.
 - ++ activity of atrial stretch R
 - Bainbridge reflex

4 Exercise

5 Excitement

6 Anger

7 Most painful stimuli

8 Inspiration $\rightarrow$ VR $\uparrow$

9 Hypoxia

10 Catecholamines (epinephrine) β Receptor

11 Thyroxine $\rightarrow$ Thyroxine

12 Fever

- HR is decreased by
 - ++ activity of arterial barorecept.
 - Fear
 - Stim of trigeminal pain fibres
 - Expiration
 - Norepinephrine
 - ++ intracranial P

VC

++ TPR

++ ABP

-- HR

reflex

مشارة

التوازن

مشتة متفرقة

الدم في الشرايين
في الجهد

$$ABP = HR \times SV \times TPR$$

Circulatory shock

- Definition: Inadequate tissue perfusion due to Inadequate cardiac output (relative or absolute)

Types & causes

- Hypovolemic shock e.g. haemorrhagic shock (Surgical), Burns (-- plasma), Dehydration (-- serum)
- Low resistance shock = vasogenic due to VD e.g. Neurogenic, anaphylactic or septic shock.
- Cardiogenic shock due to -- COP e.g. Myocardial infarction, Congestive HF or severe arrhythmia
- Obstructive shock
 - Lung problems: tension pneumothorax, massive pulm. embolism
 - Cardiac problems: cardiac tamponade, tight stenosis of valve

(2) VD

causing $\rightarrow$ ABP $\xrightarrow{\text{cause}}$ $\rightarrow$ $\uparrow$ HR except in cranial Hemorrhage.

Haemorrhagic shock نین - بے - نفس - حواس

- Manifestations $\uparrow$ HR $\uparrow$ to compensate.
- Vital signs -- ABP, rapid weak pulse, rapid respiration
- Temp cold pale clammy skin (due to symp stim.)
- Others Intense thirst (angiotensin II) & Oliguria (-- RBF)
- Acidosis (lactacidosis) Restlessness & apprehension.

Note if -- consciousness = severe shock (acidosis & cerebral ischaemia)

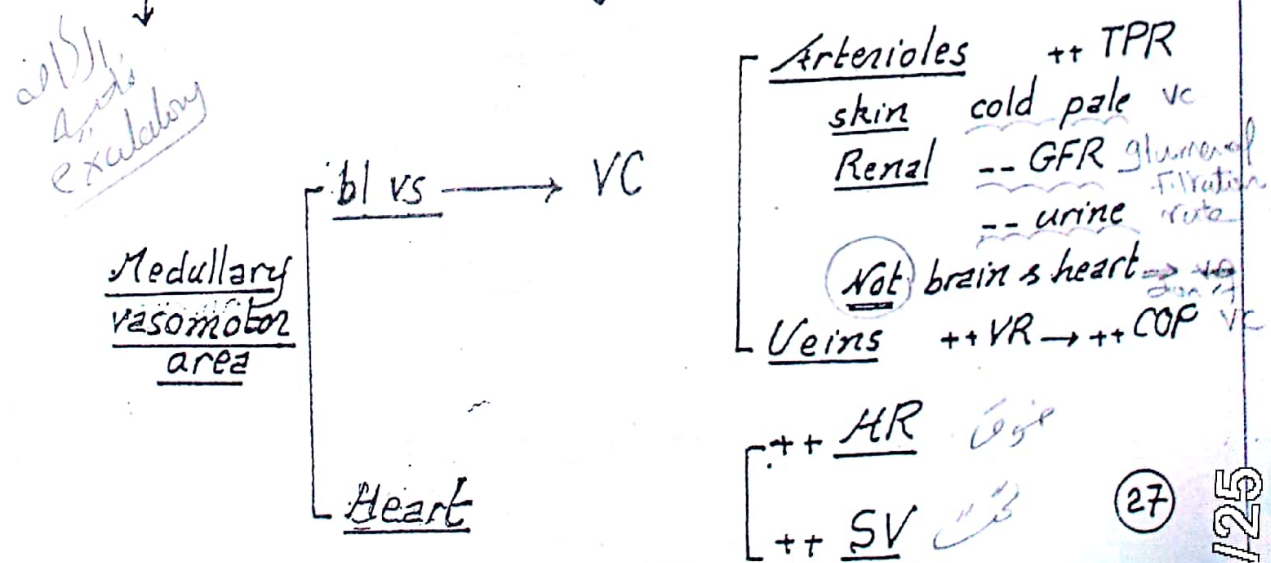
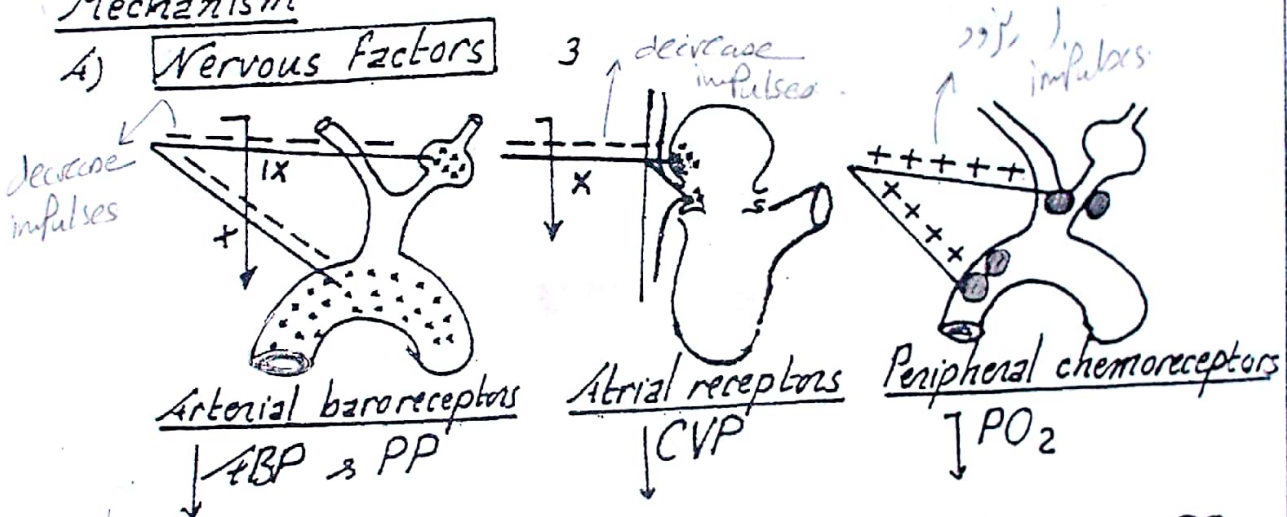
Compensatory reactions to haemorrhagic shock

1 Rapid compensatory reactions

Aim: To maintain ABP for adequate perfusion of heart & brain i.e Protective

Mechanism

A) Nervous factors



B) Humoral Factors

1) ++ Catecholamines

Cause Hypotension

limited role in ++ ABP

(Stim) RF → restlessness

reticular formation →

2) ++ Angiotensin II

Cause renal ischemia

++ ABP (discuss)

thirst → ++ ECF

3) ++ Vasopressin

Cause -- atrial R disch

++ H₂O reab by

kidneys → ++ ECF

Long term compensatory reactions

Aim To restore the blood which is lost

1) Correction of plasma vol:

12-72 hours
($\frac{1}{2}$ -3) days

a) Tissue Fluid shift

PCV & plasma ptr conc

b) Thirst sensation

c) ADH secretion is increased due to -- discharge from atrial receptor

d) Aldosterone secretion is increased due to ++ Angiotensin II & ++ ACTH

2) Correction of plasma ptrs:

3-4 days

preformed albumin

hepatic synthesis

3) Correction of red cell mass:

4-8 weeks

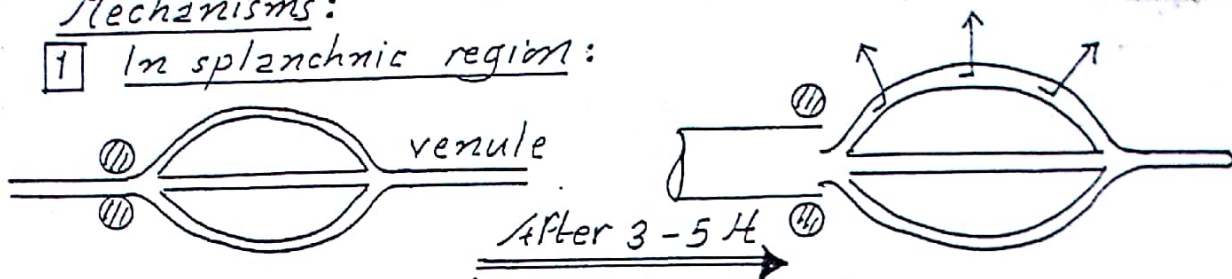
Erythropoietin hormone

● Outcome of shock state Pts may

- 1 Recover completely due to compensatory mech. or proper ttt
- 2 Die rapidly due to failure of " " or " "
- 3 Pass to Refractory (irreversible) shock
i.e COP remains low even if bl. vol. is restored to normal

Mechanisms:

[1] In splanchnic region:



Tissue hypoxia

Tissue damage O₂ radicals of granulocytes
Vaso dilatation By bacterial toxins

[2] Deadly Positive Feed back mechanisms

(a) Severe cerebral ischaemia

-- ABP → cerebral "
→ Failure of CV centres
→ -- HR & VD
→ -- ABP

(b) Severe cardiac ischaemia

-- ABP → " "
→ -- Cardiac contractility
→ -- COP
→ -- ABP

● Treatment of shock:

- 1 Removal of the cause e.g. stoppage of bleeding
- 2 Supine position with feet raised to ++ VR
- 3 Restoration of blood volume:

a. blood transfusion in haemorrhagic shock.

b Plasma " or plasma expander e.g. dextran in burns

c Concentrated human albumin. Disadvant: t dehydration

4 Drugs:

a Vasopressors : ++ ABP but -- bl. flow

b Dopamine : in cardiogenic & traumatic shock.

c Epinephrine : in anaphylactic shock.

d Glucocorticoids — capill. permeability

Special circulations

Coronary circulation

• Anatomical consideration:

• Coronary arteries Supply:

a Right :

Rt ventricle & post. wall of Lt ventricle

b Left :

anterior & lateral walls of Lt ventricle.

Major vessels lie on epicardial surface & act as low resistance vs

Systolic compression affects the subendocardial vessels

Anastomosis exists between small (not main) coronary vessels

Rt coronary receives bigger flow in 50% of people.

Lt " " " " in 20% of people.

Both arteries receive equal flow in 30% of people.

Venous drainage

Coronary sinus & ant. coronary vein drain most bl. into Rt atrium

	Cardiac muscle	Skeletal muscles
Capillary density/mm ²	3000 - 4000	500 - 2000
Bl Flow in ml/100g/min	80 84 during rest	2.7
O ₂ require. ml/100g/min	10 9.7	0.2
Vaso motion	No all capill. open	Present

During rest, myocardium extracts 70 to 80% of O₂ in coronary bl.
During exercise, Coronary bl. flow must ++ to supply the extra O₂

• Regulation of coronary bl. flow: 2 factors

A) Coronary Perfusion Pressure

$$= \text{Aortic pressure} - \text{ventricular (not venous) pressure}$$

	During	Aortic P	-	Vent P	=	Gradient in mmHg
Lt ventricle	Systole	121	-	120	=	1
	Diastole	80	-	0	=	80 →
Rt ventricle	Systole	120	-	25	=	95
	Diastole	80	-	0	=	80 → (30)

WAP

2012/08/25

B) Coronary vascular resistance is regulated by 4 factors

1 Metabolic regulation:

++ cardiac activity $\rightarrow$ ++ metabolites $\rightarrow$ activate ATP sensitive K channels
PGs & adenosine $\rightarrow$ activate ATP sensitive K channels
in smooth ms of coronary vs $\rightarrow$ hyperpol. $\rightarrow$ relaxation $\rightarrow$ VD

2 Endothelial regulation:

a Vasodilator substances e.g. prostacyclin & NO
b Vasoconst. substances e.g. endothelin 1

In response to Mechanical stimuli (e.g. shear stress) $\rightarrow$ ++ NO (change)

3 Nervous regulation:

a Symp. stim. $\rightarrow$ α receptors $\rightarrow$ VC
Noradrenaline α/β $\rightarrow$ β receptors $\rightarrow$ VD

However ++ HR & contractility $\rightarrow$ ++ metabolites $\rightarrow$ VD

b Parasymp stim $\rightarrow$ cholinergic receptors $\rightarrow$ VD
ACholine $\rightarrow$ No $\rightarrow$ VD

However -- HR $\rightarrow$ -- metabolites $\rightarrow$ VC

4 Autoregulation:

CBF is kept $\pm$ with ABP changes between 40 & 130 mmHg
It depends on myogenic response, local metabolites & substances released from endothelium e.g. NO.

• Measurement of CBF

1 Kety method Fick's principle

Using inhaled N₂O
$$CBF = \frac{Q \times}{[A_x] - [V_x]}$$

Q x N₂O taken by heart/min
A x N₂O arterial concentration
V x N₂O venous concentration

2 Radio nuclides techniques

a Thallium 201 pumped in cardiac ms by Na-K ATPase.
201 Tl distribution $\propto$ myocardial bl. flow
Areas of ischaemia detected as COLD spots
b Technetium 99m infarct areas detected as HOT spots

3 Coronary angiography by radio-opaque dye

012/08/25

Pulmonary circulation

• Anatomical considerations

- Lungs only organ receive the whole COP
- Bronchial arteries to bronchial tree are branches of systemic circ
- VR of " vessels $\rightarrow \frac{1}{3}$ Rt atrium & $\frac{2}{3}$ Lt atrium.
- Extra-alveolar vessels: branches of pulm. & parallel to bronchi & bronchioles
- Alveolar vessels: capillaries around alveoli
- Compared to systemic circ, PULMONARY $P_{aorta} \approx 120/80$ $P_{pulm} \approx 25/10$

Pressure (mmHg)	Resistance	Vessels	Venous bl.	Blood gases
	Main site is <u>capillaries</u> not arterioles $R = \frac{\Delta P}{F}$ $= \frac{7}{5}$ $= 1.4$ mmHg/L/min i.e. much less	Thinner & contain less smooth muscles Pulm. a $\frac{1}{3}$ thickness of aorta Note Rt vent. $\frac{1}{3}$ thickness of Lt vent.	Oxygenated (not reduced blood)	PO_2 5 PCO_2 ++ produce VC (not VO) So, bl. shifts from poorly to well ventilated alveoli

• Factors affecting pulmonary vascular resistance PVR

1 Lung volume

- PVR is minimal at functional residual capacity FRC

Volume	R of extra alveol vs	R of alveolar vs	net PVR
TLC	- (more -ve pleural p)	+ (alveoli expand)	++
RV	+ (less -ve " p)	- (alveoli collapse)	++

2 Volume of bl in pulmonary vs

- PVR $\propto$ Flow ++ to limit ++ in pulm. pressure

Mechanism Distension of thin walled pulm. vs

Recruitment of opened capill.

(32)

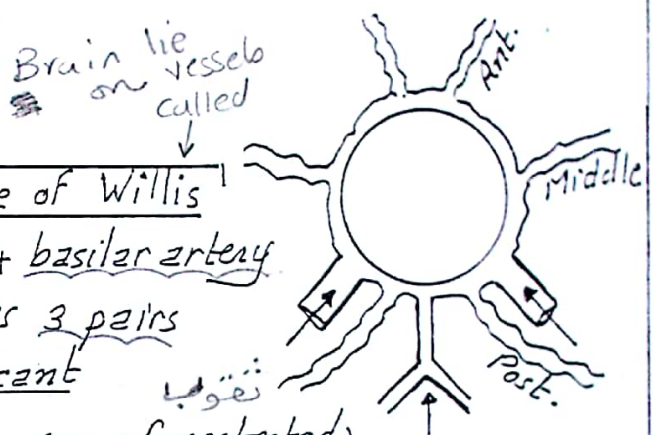
- 3 -- Alveolar PO_2
- 4 ++ Alveolar PCO_2
- 5 Autonomic innervation Symp stim. ++ PVR → -- bl. flow
 eruvoo ← Noradrenaline → α cereb. artery
- 6 Vasoactive substances Humoral ← Regulation
 ↓ VC → ++ P
- a Vasoconstrictors norepinephrine, angiotensin II, (ETs), histamine & serotonin.
- b Vasodilators (Acetylcholine), (ANP), bradykinin & NO
- Note Pt with pulm. hypertension, has -- NO synthase

Ring of Rire

Cerebral circulation

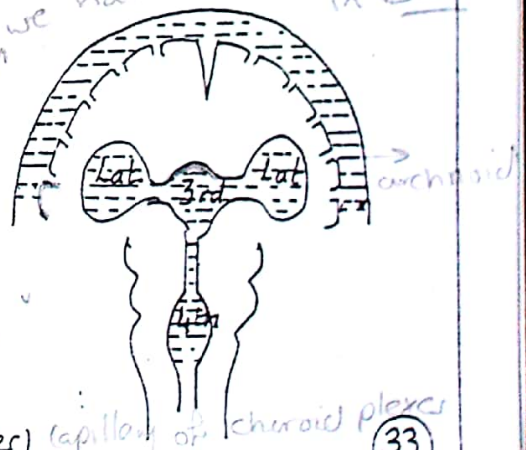
Anatomical considerations

- Arterial blood : circle of Willis
 Formed 2 internal carotid + basilar artery
 Gives 6 cerebral arteries 3 pairs
 Anastomosis is insignificant
- Capillaries continuous (non fenestrated)
- Venous drainage Deep veins & dural sinuses → internal jugular vein
- Innervation Ganglion Ch. transmitters
 a Symp Superior cervical Norepin. & neuropeptide Y
 b Parasymp Sphenopalatine Acetylcholine
 c Sensory Trigeminal



Cerebrospinal Fluid CSF

- Site : Brain ventricles
 Subarachnoid space
- Volume: 150 ml (cm^3)
- Rate of Formation: 550 ml/day
- Formation :
 a 70% choroid plexus (capillaries)
 b 30% around cerebral vs & from ventricular wall



- Circulation: Lat. ventricles $\rightarrow$ 3rd vent. $\rightarrow$ 4th vent. $\rightarrow$ subarachnoid space (between pia & arachnoid matter)
- Absorption: Arachnoid villi to venous sinuses
Largely by bulk flow

Pressure: 7-18 cm H₂O not mmHg

++ P $\rightarrow$ ++ absorp Absorption stops at 7cm H₂O

Composition of CSF = brain interstitial fluid

Compared to plasma

- Same Osmolarity, Na^+ & HCO_3^- conc.
- More Mg^{++} , Cl^- & Creatinine conc.
- Less Pln , Glucose, K^+ , Ca^{++} , inorganic $PO_4^{=}$, urea, uric acid, lactic acid & cholesterol.

Functions

- 1 Protective brain is supported in arachnoid by
 - a H₂O bath of CSF -- brain weight from 1400 to 50 g
 - b Blood vessels & nerve roots
 - c Fine Fibrous arachnoid trabeculae

These 3 mech. protect brain against head trauma.

- 2 Medium delivers substances (nutrients, transmitters & drugs)
- 3 Sink receives waste metabolic products

Blood-brain barrier BBB

- Definition: Barrier limits movements of substances between Capill. bl to brain & CSF

N.B movement in opposite direction is more free

- BBB is due to: tight junctions between, Capill endothelial cells & Choroid epith. cells
- Movement of substances $\propto$ Lipid solubility

e.g. rapid cross:

H₂O, CO₂, O₂
Glucose (main fuel)
due to transporter

slow cross: H^+ , HCO_3^-
Pln & Pln bound subst.

- Development of BBB First few years of life
In infant, bilirubin reaches brain → kernicterus
Kern → ectrus
- Functions

- ① Maintains brain environment constant
- ② Protects brain from lipid insoluble toxins in blood
- ③ Prevents escape of neurotransmitters to blood

Circumventricular organs

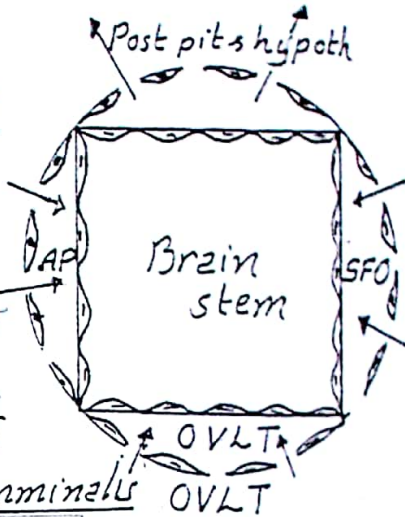
4 small areas around brain stem
no BBB (fenestrated capillaries)

- ① Post. pit. & median eminence of hypoth.
secrete hormones directly in blood

2 Area postrema CRTZ
blood changes → vomiting center

3 SubFornical organ.
stim. by angiotensin II → Thirst

④ Organum vasculosum of lamina terminalis
site of osmoreceptors controlling ADH



- BBB is disrupted by marked ++ ABP, infection, injury or tumours

● Cerebral blood flow CBF

- Measurement:

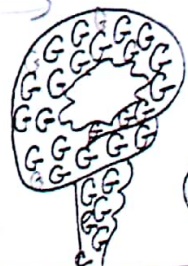
① Kety method Fick's principle inhaled N_2O
$$CBF = \frac{Q_x}{[A_x] - [V_x]}$$
 refer to coronary bl. flow

Normal standard 55 ml/100g/min Whole brain 750 ml/min

No information about regional blood flow.

Regional blood flow is measured by:

② Positron emission tomography (PET)
Blood flow & metabolic activity
Using 2 deoxy glucose labeled with positron emitter is injected in bl.



35

2012/08/25

3 Functional magnetic resonance imaging fMRI

OxyHb & DeoxyHb produce different resonance signals

Average bl. flow in gray matter 69 ml/100 g/min.

in white matter 28 ml/100 g/min.

Regulation of cerebral circulation

15% of COP

20% of total O₂ consumption

Marked Fluctuation in different brain areas

However regulation keeps total bl. flow constant.

Factors regulating cerebral blood flow:

1 Metabolic regulation (most important)

CBF $\propto$ metabolic activity

viz vasodilators mediators e.g. H⁺, CO₂, K⁺ & NO

2 Arterial PCO₂

CBF $\propto$ arterial PCO₂

linear relation with PCO₂ From 20 to 80 mmHg

++ PCO₂ $\rightarrow$ [H⁺] in brain interstitial fluid + NO

$\rightarrow$ -- intracell. Ca⁺⁺ in vascular smooth ms $\rightarrow$ VD

3 Arterial PO₂

Moderate changes in arterial P O₂ doesn't affect CBF

Marked -- PO₂ below 50 mmHg $\rightarrow$ ++ CBF (via adenosine)

4 Autoregulation

It keeps CBF $\pm$ with ABP between 65-140 mmHg

Mechanism Myogenic or Metabolic (Mechanism imp.)

5 Neural regulation

However, ++ ABP $\rightarrow$ ++ symp VC $\rightarrow$ $\pm$ CBF (autoreg)

Role of intracranial pressure (ICP)

Cushing reflex ++ ICP e.g. cerebral hge $\rightarrow$ ++ ABP $\rightarrow$ -- ICP

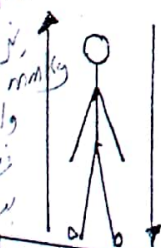
++ ABP maintains $\pm$ CBF until ICP is markedly ++

Vertical (upward & downward) acceleration

++ cerebral venous pressure $\rightarrow$ ++ ICP $\rightarrow$ -- CBF

-- ICP $\rightarrow$ ++ CBF

++ CBF



upward
lower part of body

--

Blackening out

ischemia & loss of consciousness

-- intracranial pressure

-- to oppose the effect of -- ABP

Acceleration

Blood moves to
ABP at head

CBF

Phenomenon

Cerebral

Compensations:

Venous P & ICP

P on cerebral vs

Downward

Upper part of body

++

++

Reddening

may rupture of vessels

++

++ protecting them from rupture

Cutaneous circulation

Cutaneous circulation

2 types

1 Nutritive vs : Ordinary arterioles, capill & veins

2 Vessels concerned with heat regulation

a Subcutaneous venous plexus holds large vol of bl to heat skin

b Arterio-venous anastomosis between arterioles & venous plexus

Site palm, sole, lips, nose and ears

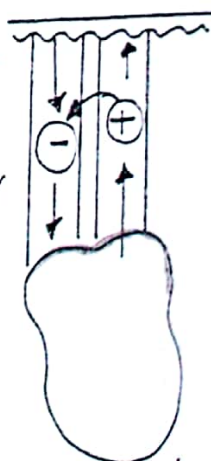
They have strong muscles supplied by symp adrenergic vasoconstr.

In cold, they constrict → -- bl. flow to plexus → -- heat loss

The counter current heat exchange mechanism

Arterial blood to extremities gives some heat to cold blood in adjacent vein

Result cooling of bl. to peripheral areas of body
warming of bl. reentering body core



Regulation of cutaneous circulation

1 Effect of sympathetic innervation

a Symp adrenergic Fibres

VC of skin arterioles

b Symp cholinergic Fibres

VD

++ secretion of sweat glands via kinins

So intense symp stim. in hge, skin is pale (VC) clammy (sweat)

2 Effect of environmental & body temp.

(a) ++	environmental & body temp	(b) --
	Thermoreceptors (skin & hypoth)	
dilatation of skin vs	initiate reflex	constriction of skin vs
Gain	to minimise heat	Loss

However, very low skin temp blocks nerve impulse $\rightarrow$ VD of vessels to prevent tissue freezing.

(c) Direct application of heat to skin $\rightarrow$ VD & vice versa
It occurs in denervated skin i.e. not reflex

(d) During m. exercise, body temp ++ & skin vessels dilate in spite of ++ symp activity

3 Response to mechanical stimuli

- a White reaction (line) Discuss
- b Triple response Discuss

Afferent nerve fibres of different receptors

sneezing R

swallowing arterial baroreceptors

Coughing R peripheral chemorec.

Stretch R arterial barorec.

Lung irritant R periph. chemo

J receptors

GIT receptors

Micturition R

Defecation R

Erection R

head

neck

thorax

Abdomen

pelvis

Trigeminal n

Glossopharyngeal n

VAGUS

pelvic

Good Luck

(38)